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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,660	01/10/2005	Hiromu Habashita	Q85692	7023
65565	7590	03/05/2008		
SUGHRUE-265550 2100 PENNSYLVANIA AVE. NW WASHINGTON, DC 20037-3213			EXAMINER MURRAY, JEFFREY H	
			ART UNIT	PAPER NUMBER
			1624	
			MAIL DATE	DELIVERY MODE
			03/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/520,660	Applicant(s) HABASHITA ET AL.	
	Examiner JEFFREY H. MURRAY	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 January 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-33,35-43 and 46-49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-33,35-43 and 46-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/10/2005, 5/19/2005, 11/9/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. This action is in response to a restriction election filed on January 10, 2008. There are forty-eight claims pending and forty-five claims under consideration. Claim 45 has been cancelled. Claims 3, 34 and 44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. The applicants have elected Group I **without** traverse. Election was made **without** traverse in the reply filed on January 10, 2008. This is the first action on the merits. This invention relates to a compound having CCR4 antagonistic activity which is useful as a medicament, a method for producing the same, and use thereof.

Applicants have pointed out to examiner, that claim 45 was cancelled before the restriction requirement was sent out. Claim 45 appears in Group V of the restriction requirement. Accordingly, Group V will be eliminated and the restriction requirement will only contain Groups I-IV.

Claim 3 above was inadvertently added to Group I during the restriction requirement. Claim 3 covers compounds or compositions in which "Ring D" is a carbocyclic ring whereas applicants have elected Group I, in which "Ring D" is a 1,4-diazine, or a pyrazine ring. Since Claim 3 only covers a carbocyclic ring, and applicants have elected where Ring D is a heterocyclic ring, Claim 3 does not cover the elected subject matter, and is hereby declared withdrawn.

Priority

2. Acknowledgment is made of Applicant's claim for foreign priority. This application, U.S. Application No. 10/520,660, filed on January 10, 2005, is a national stage application of PCT/JP03/08654, filed on July 8, 2003, claims foreign priority to Japanese Application No. 2002-200879, filed July 10, 2002.

Specification

3. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any of the errors of which applicant may become aware of in the specification.

Claim Objections

4. Applicant is advised that should claim 1 be found allowable, claims 35-43 and 47-49 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof.

When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

5 Claim 26 is objected to because of the following informalities: Claim 26 ends with a comma and not a period. Under MPEP 608.01(m), "Each claim begins with a capital letter and ends with a period." Appropriate correction is required.

Claim Rejections - 35 USC § 112, 1st paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

Art Unit: 1624

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 2, 4-32, 35-43, and 46-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the

Art Unit: 1624

claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient."

MPEP § 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Fiers, 984 F.2d at 1171, 25 USPQ2d 1601; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*,

the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a compound having CCR4 antagonistic activity which is useful as a medicament, a method for producing the same, and use thereof. The factors considered in the Written Description requirement are the following:

1) *Level of skill and knowledge in the art.* With regards to the effect of synthesizing and substituting various ring systems, the level of skill is high, and the knowledge is low, as the chemistry of attaching potentially sterically bulky or electronically unstable rings to other rings of the same are unpredictable based on the substituent groups, electronic effects, steric effects, etc.

2) *Partial structure.* The structure must be a cyclic ring system attached to two other cyclic ring systems either directly or with a 1-8 atom linker. The specification describes a few hundred species which lack sufficient variety to describe the myriad of possible ring systems embraced by the generic structure.

3) *Physical and/or chemical properties and (4) Functional characteristics.* The peptides must have CXCR4 antagonizing activity and be useful for preventing inflammatory and/or allergic diseases.

5) *Method of making the claimed invention.* Methods of making multiple ring systems are well known in the art, however the methods of making the myriad of compounds within the asserted claims are not known. Further, there is no disclosure as

to what is the essential structure that must be maintained throughout the compounds to retain the claimed activity.

As stated supra, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim 1, for example, is a broad generic, with respect to all possible ring systems attached to two other ring systems either directly or by a linking group. The possible structural variations are limitless within this claim, where all three ring systems are defined by generic structures. Though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of ring systems outside of D being a pyrazine ring. While having written description of the pyrazine ring core of claim 33, the specification is void of sufficient variety of ring systems to describe the myriad embraced by the genus.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide

Art Unit: 1624

adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

8. Claims 1, 2, 4-33, 35-43, and 46-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 2,3-disubstituted pyrazine rings, where the 2-position is attached to an oxygen and optionally a linker of atoms with a ring, and the 3-position is attached to an aminosulfonyl group attached directly to a thienyl or phenyl group which is optionally substituted with alkyl, halogen, alkoxy, haloalkoxy cyano or nitro groups, does not reasonably provide enablement for all other compounds not previously mentioned. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

9. The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (*United States v. Teletronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988)).

These factors include the following:

1) *Amount of guidance provided by Applicant.* Applicant has provided no guidance, examples, or provided any chemical or biological data and/or testing results

Art Unit: 1624

of any compounds other than previously mentioned. Applicants have shown a large number of compounds or compositions within the specification and of these, none of them fall outside of the scope of enablement mentioned here.

2) *Unpredictability in the art.* Chemistry is unpredictable. See *In Re Marzocchi* and Horton 169 USPQ at 367 paragraph 3:

“Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work ...Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious) ...” Dorwald F. A. *Side Reactions in Organic Synthesis*, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

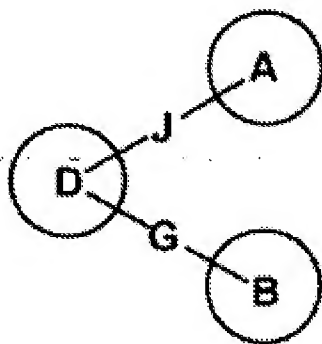
The scope of any compounds where the variables are not those previously described above is not adequately enabled or defined. Applicants have provided no guidance as how the compounds are made more active *in vivo*.

3) *Number of working examples.* . Applicant has provided no working examples of any compounds or compositions other than those described above. “Specific operative embodiments or examples of the invention must be set forth. Examples and

description should be of sufficient scope as to justify the scope of the claims. *Markush* claims must be provided with support in the disclosure for each member of the *Markush* group. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula." See MPEP 608.01(p).

4) *Nature of the invention.* The nature of this invention relates to a compound having CCR4 antagonistic activity which is useful as a medicament, a method for producing the same, and use thereof.

5) *Scope of the Claims.* The scope of the claims is all of the millions of compounds represented by general formula (I):



thus the scope of the claims is very broad.

6) *Level of skill in the art.* The artisan using Applicants invention would be a chemist with a M.S. or Ph.D. degree, and having several years of bench experience.

MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make

Art Unit: 1624

and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here that Applicant is not enabled for making these compounds or compositions.

Claim Rejections - 35 USC § 112, 2nd paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 36-43 and 46-49 are rejected under 35 U.S.C. 112,second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of an intended use, chemical activity, or functional description of some "additional" property for a compound (or moiety/functionality attached to a chemical core) or a composition containing same in a dependent claim, must result in a tangible structural difference between the product and of the independent claim and the product set forth in the dependent claim. In the absence of said structural difference between the product of the independent claim and that of the dependent claim, said dependent claim is seen to be a substantial duplicate, and said recitation is not afforded critical weight and fails to further limit the product in said dependent claim. In the instant set of claims, claims 36-43 and 46-49 fail to further limit the claims to compositions from which they depend.

Art Unit: 1624

Claim Rejections - 35 USC § 102

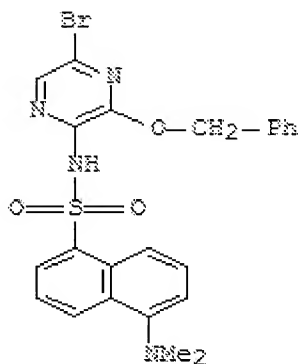
12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 2, 4-8, 10, 12, 14, 16, 18, 20, 22-26, 30-33, 35-43, and 46-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Bradbury, et. al., Journal of Medicinal Chemistry (1997), 40(6), 996-1004. The prior art contains a compound #71 on page 999, with the following structure:

RN 187973-57-5 CAPLUS
 CN 1-Naphthalenesulfonamide, N-[5-bromo-3-(phenylmethoxy)pyrazinyl]-5-(dimethylamino)- (SCI) (CA INDEX NAME)



where the D ring is a pyrazine ring, A represents a phenyl ring and B represents a naphthyl ring. J is an oxygen with a CH₂ group, G represents an aminosulfonyl group. R¹ represents bromine, R² represents hydrogen, p=0, q=1 and R₆ is a dimethylamino group.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1, 2, 4-33, 35-43, and 46-49 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-28 and 30 of U.S. Patent Publication Application No. 2007/0254886. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-28 and 30 of U.S. Patent Publication Application No. 2007/0254886 embrace the instant claims 1, 2, 4-33, 35-43, and 46-49.

The instant claim differs from the copending claim by a more limited genus than the claim of the copending application. However, it would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus of the copending application, including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus of the copending application since such compounds would have been suggested by the claims of the copending application. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. v. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

16. Claims 1, 2, 4-33, 35-43, and 46-49 are rejected.
17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is (571) 272-9023. The examiner can normally be reached on Mon-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a US PTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H Murray/
Patent Examiner
Art Unit 1624

James O. Wilson
Supervisory Patent Examiner
Art Unit 1624

Application/Control Number: 10/520,660
Art Unit: 1624

Page 16